Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Initially, applicants note that the U.S. Patent and Trademark Office ("PTO") has improperly and unilaterally altered the prior election of species. In the original election, applicants were required to elect for Group I a single tissue-reactive functional group and whether the material that comprises the tissue reactive functional group is formed by derivatization of a polymer precursor. If so, applicant was then required to elect a specific polymer precursor or a specific combination of polymer precursors. See Office Action dated February 26, 2008, at page 4. There was no requirement to elect a species of the polymerisable and/or cross-linkable material. In response, applicants elected N-hydroxysuccinimide ("NHS") esters as the tissue-reactive functional group and a material formed by derivatization of a polymer precursor, where the derivatized polymer is a co-polymer of N-vinyl-2-pyrrolidone and acrylic acid ("PVP-co-PAA"). The claims of Group I reading on these elected species are claims 1–10, 12–22, and 28–30. Acknowledgement of this election was made in the April 8, 2008, Office Action and all of claims 1–10, 12–22, and 28–30 were considered. In the October 31, 2008, Office Action, the PTO considered these same claims.

Now, after two office actions on the merits and the filing of a Request for Continued Examination, the PTO asserts at page 2 of the outstanding Office Action that the search was expanded to non-elected embodiments, though not to the entire scope of the claims. Despite this assertion, the PTO has failed to examine claims 8–10, 13–19, and 22, which read on the previously elected species, by unilaterally modifying applicants' prior election. This is not only improper, it makes no sense insofar as the search was to be expanded. How can an expanded search scope omit the elected species? It should not. Moreover, if the PTO now requires an election of the polymerisable and/or cross-linkable material, it is applicants who make the election, not the PTO. 37 C.F.R. § 1.146. Applicants were not previously required to make such an election and the PTO must afford applicants the opportunity to do so. In an effort to expedite prosecution, to the extent that the PTO now requires election of a polymerisable and/or cross-linkable material as recited in claim 23, applicants elect albumin as the species. Claims of Group I reading on all of the elected species include pending claims 1–7, 17–22, and 27–30.

For these reasons, all of claims 1–7, 17–22, and 27–30 as presented should be examined.

Claims 1, 6, 17–19, and 27 have been amended and claims 8–11, 13–16, and 23–26 have been cancelled without prejudice. Support for the amendment to claim 1 is found on page 9, lines 5–6; page 12, lines 20–26; page 13, lines 9–13; and original claims 16 and 26. Accordingly, no new matter has been added. As noted above, applicants previously elected PVP-co-PAA and NHS, and hereby further elect albumin.

Claims 1–7, 17–22, 27–44, 53, and 63–67 remain pending, with claims 31–44, 53, and 63–67 being properly withdrawn and claims 17–19, 22, and 27 being improperly withdrawn for the reasons discussed above.

The objection to claim 6 under 37 C.F.R. § 1.75(c) for being in an improper dependent form is respectfully traversed.

Claim 1 recites "a tissue-adhesive formulation comprising a naturally occurring or synthetic polymerisable and/or cross-linkable material in particulate form, the polymerisable and/or crosslinkable material in admixture with particulate material comprising tissue reactive groups." The term "comprising" in claim 1 is open-ended and indicates that the tissue-adhesive formulation of claim 1 contains at least one particulate material, but may contain more than one particulate material. Therefore, because claim 6 further limits the tissue-adhesive formulations of claim 1 to those formulations containing only one particulate material, it is now in proper dependent form. This objection should therefore be withdrawn.

The rejection of claims 1–7, 20, 21, 24, 29, and 30 under 35 U.S.C. § 112 (first para.) for failure to comply with the written description requirement is respectfully traversed in view of the above amendments to claim 1 and the following remarks. The PTO has acknowledged at page 6 of the Office Action that the specification provides descriptive support for formulations containing NHS-activated PVP-co-PAA with albumin. However, a number of other suitable tissue-reactive functional groups are identified at page 10, line 30, to page 11, line 19 of the specification. These suitable tissue-reactive functional groups include those functional groups capable of reaction (under the conditions prevalent when the formulation is applied to tissue, i.e., in an aqueous environment and without the application of significant amounts of heat or other external energy) with functional groups present at the surface of the tissue. The latter class of functional group includes thiol and amine groups, and tissue-reactive functional groups

therefore include groups reactive to thiol and/or amine groups. Examples include imido ester, p-nitrophenyl carbonate, NHS ester, epoxide, isocyanate, acrylate, vinyl sulfone, orthopyridyl-disulfide, maleimide, aldehyde, and iodoacetamide, although NHS ester is identified as preferred.

Because the specification explicitly recites a number of tissue-reactive functional groups that can replace NHS, a person of skill in the art would fully appreciate that applicants were in possession of the invention as claimed. The PTO has not cited any basis why the skilled person would not reach this same conclusion with respect to admixtures of albumin and functional-group activated PVP-co-PAA as claimed. Therefore, the rejection of claims 1–7, 20, 21, 24, 29, and 30 for lack of written description should be withdrawn.

The rejection of claims 1–4, 6–7, and 29–30 under 35 U.S.C. § 103(a) for obviousness over U.S. Patent No. 6,989,192 to Husemann et al. ("Husemann") is respectfully traversed in view of the amendments above and remarks below.

Husemann teaches a process for preparing crosslinked polyacrylate pressure sensitive adhesives. The process is preferably used for preparing crosslinked polyacrylate pressure sensitive adhesives containing polymer particles that assist the crosslinking reaction of the polyacrylates. The cohesion of the pressure sensitive adhesive is modified by the crosslinking, and where polymer particles having a high transition temperature are used, the viscoelastic properties are modified by incorporation of the polymer particles. Husemann does not disclose or suggest a tissue-adhesive formulation containing a combination of albumin and PVP-co-PAA derivatised with tissue-reactive functional groups as recited in claim 1.

The polyacrylate adhesives of Husemann are described for general industrial use. Industrial tapes are conventionally used for adhering to dry surfaces, most commonly to hard, dry surfaces. This is supported by the fact that adherence is determined in Husemann by measurement of the bond strength to steel (Test A). Accordingly, there is no reason for the skilled person to consider the polyacrylate adhesives described by Husemann for application to wet substrates.

In contrast, the present invention is concerned with formulations that are suitable for application to internal tissue surfaces such as the surfaces of internal organs exposed during surgical procedures, including conventional and minimally invasive surgery. Without evidence to the contrary, the skilled person would consider the polyacrylate adhesives of Husemann to be unsuitable for internal medical applications.

The formulations described in Husemann and the formulations of the present application are fundamentally different. The formulation of the present invention is designed to exhibit a chemical interaction with the surface of the tissue which it is put into contact, by virtue of the tissue-reactive functional groups present on the PVP-co-PAA. However, the polyacrylate adhesives of Husemann are designed to adhere to steel (see Test A and Table 1), which does not involve a chemical interaction with the steel. Husemann fails to provide a skilled person any reason to use the described polyacrylate adhesives for applications requiring a different mechanism of adherence. Indeed, a skilled person would not expect that an adhesive suitable for adherence to steel or the like in industrial applications would be a suitable starting point for the development of an adhesive for application to exposed tissues in medical applications.

Husemann describes an improved process using known materials that are established and proven to be advantageous in the preparation of polyacrylate adhesives of this type. There is absolutely no motivation provided by Husemann for a skilled person to use materials other than the polyacrylates and additives described therein.

In particular, Husemann provides no reason for the skilled person to incorporate a protein (*i.e.*, albumin) into the tissue-adhesive formulations of the present invention. Apart from the relatively high cost and limited availability of proteins on the scale that would be required for the manufacture of an industrial tape, it is clear that proteins would be denatured in the hot melt process described in Husemann, and hence would be entirely unsuitable for use in that process.

Because Husemann provides no reason for the skilled person to adapt the described adhesives by incorporating albumin and PVP-co-PAA derivatised with tissue-reactive functional groups, the claimed invention would not have been obvious. The rejection of claims 1–4, 6–7, and 29–30 in view of Husemann is improper and should be withdrawn.

The rejection of claims 1, 4–7, 24, and 29 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent Publication No. 2002/0106409 to Sawhney et al. ("Sawhney") is respectfully traversed for several reasons.

Firstly, Sawhney was not published more than one year before the April 4, 2003, priority filing date for the present application. Therefore, Sawhney is not available as prior art under 35 U.S.C. § 102(b). Secondly, for the reasons discussed below, Sawhney does not teach or suggest the presently claimed formulation.

Sawhney refers to the use of dehydrated precursors for forming hydrogels *in situ*. The hydrogels are described for a variety of medical applications, including use as tissue sealants. Sawhney discusses the use of dry precursors in general, and, in particular, the advantages of using dry precursors which activate on exposure to fluid in a physiological environment compared to the use of solutions for *in situ* therapy. However, there are only a small number of specific precursors described in Sawhney (*see* Examples). Sawhney does not disclosure a particulate formulation containing a combination of albumin and PVP-co-PAA derivatised with tissue-reactive functional groups as recited in claim 1 of the present application.

Although Sawhney attempts to solve the same problem as the present invention, *i.e.*, the problem associated with the use of solutions *in situ*, by using dry particulate precursors, it provides an alternative and distinct combination of precursors as the solution to this problem.

There is nothing in Sawhney to direct a person skilled in the art to the specific combination of materials recited in claim 1. Accordingly, the rejection of claims 1, 4–7, 24, and 29 under 35 U.S.C. § 102(b) over Sawhney is improper and should be withdrawn.

In view of all of the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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